The role of laparoscopy in the management of borderline ovarian tumors

Dissertation
zur Erlangung des akademischen Grades

doctor medicinae (Dr. med.)

vorgelegt dem Rat der Medizinischen Fakultät
der Friedrich-Schiller-Universität Jena

von Askin Dogan

geboren am 19.05.1978 in Istanbul

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Tag der öffentlichen Verteidigung: 4.12.2012

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Jena, den 28.2.2012 Askin Dogan

Index

Zusammenfassung 6

1. Summary 9

2. Introduction 11

2.1. Bordeline Ovarian Tumors (BOT) from the historical point of view ... 11
2.2. Definition of BOT 11
2.3. Incidence and etiology of BOT 12
2.4. Histology & Tumor Staging 14
2.5. Clinical findings prior to diagnosis 14
2.6. Therapy 15
2.6.1. Operative Staging 15
2.6.2. Conservative or radical surgery 15
2.6.3. Prognosis of BOT 16
2.7. Laparoscopy 17
2.7.1 Laparoscopic management of ovarian tumors and BOT 17

3. Aims of the study 18

4. Patients and Methods 19

4.1. Patients 19
4.2. Methods 19
4.3. Statistics 20

5. Results 22

5.1. Patients characteristics 22
5.2. Operative procedures: Laparoscopy vs. laparotomy 24
5.3. Recurrence of BOT 28
5.4. Survival 32
5.5. Fertility sparing treatment and pregnancy outcomes 33
5.6. Complications followed by surgery 34

6. Discussion 35

7. Conclusion 39

8. References 40

9. Supplement 48

Abreviations 48
Presented Abstracts 49
Curriculum vitae 50
Acknowledgments 51

Zusammenfassung

Einleitung: Die Borderline-Ovarialtumoren (BOT) sind eine seltene Tumorentität, die klinisch und histologisch zwischen benignen und malignen Ovarialtumoren eingeordnet werden muss. BOT werden bislang nur an wenigen Einrichtungen durch laparoskopisches „Staging“ und laparoskopische Fertilitätserhaltende oder radikale Operation behandelt. Ziel der vorliegenden Arbeit war die prospektiv geplante Untersuchung der Einflüsse verschiedener Prognosefaktoren auf das rezidivfreie Überleben und das Gesamtüberleben der Patientinnen, die Erfassung der prä- und postoperativen Komplikationen sowie die Beurteilung des Therapieerfolges nach laparoskopischen Operationen im Vergleich zum operativen Vorgehen per laparotomiam anhand von retrospektiven Daten. Darüberhinaus sollte eine systematische Evaluierung der fertilitätserhaltenden Therapie für BOT Patientinnen durchgeführt werden.

Patienten und Methoden: Die Analyse basierte auf den relevanten Daten der 60 Patientinnen mit einem Borderline-Tumor des Ovars, die in der Klinik für Frauenheilkunde und Geburtshilfe am Universitätsklinikum Jena im Zeitraum von 1996 bis 2011 behandelt worden sind. 45 Patientinnen wurden durch Laparoskopie und 15 Patientinnen durch Laparotomie behandelt. Während 31 Patientinnen radikal operiert wurden, erfolgte bei 16 Patientinnen aufgrund bestehenden Kinderwunsches die fertlitätserhaltende Operationsmethode.
Folgende Parameter wurden entsprechend dem Plan dieser Untersuchung erfasst: Tumorgröße, histologischer Typ, CA125-Wert, Operationsdauer, Dauer des Kliniksaufenthaltes, Art und Anzahl der Komplikationen, Rezidiv und Follow-up.
Eine radikale operative Therapie war definiert über die Hysterektomie, bilaterale Salpingo-Oopherektomie und infrakolische Omentektomie. Die fertilitätserhaltende Therapie beinhaltete das Erhalten von Uterus und Eierstockgewebe von einem oder beiden Adnexen. Diese Daten wurden miteinander verglichen und statistisch ausgewertet.

Ergebnisse: Das Durchnittsalter des Patientenkollektivs betrug 47 Jahre (16-78). Die Grösse der Tumoren war durchschnittlich 60 Millimeter (40-140mm) und der Mittelwert von CA125 war 31.8 (3.9-332) U/ml. Median Follow-up war 98 Monate. Insgesamt wurde in 9 Fällen von der Laparoskopie auf die Laparotomie umgestiegen. Darunter 3 Fälle aufgrund des dringenden Verdachts auf Malignität, einmal wegen der Tumorgrösse, 3 Fälle wegen der intraoperativen Ausbreitung von mindestens Stage FIGO III, 1 wegen ausgeprägten Adhäsionen und 1 wegen Komplikationen.
Die Rezidivrate war insgesamt 11,6 % (7/60). Das Gesamtüberleben war insgesamt 95% und krankheitsspezifische Gesamtüberleben war 98,3 %. Es gab keine statistisch signifikante Unterschiede bezüglich Komplikationsrate, Rezidivrisiko und krankheitsspezisfisches Überleben zwischen Laparoskopie und Laparotomie. Bei 16 Patientinnen im reproduktionsfähigen Alter wurde die fertilitätserhaltenede Therapieopition durchgeführt (13 durch Laparoskopie, 3 durch Laparotomie). Nach einer radikalen Therapie wurden 3 Rezidive und nach einer konservativen Therapie wurden insgesamt 4 Rezidive festgestellt. Das Rezidivrisiko in der Gruppe der konservativen Therapie war 2-mal höher als in der Gruppe der radikalen Therapie, jedoch statistisch nicht signifikant (p= 0,42; Fisher exact test). Es wurde kein statistisch signifikanter Unterschied bezüglich Rezidivrisiko zwischen der Laparoskopie- und Laparotomie-Gruppe gefunden. Insgesamt wurden 4 spontane komplikationslose Schwangerschaften von 4 der Patientinnen ausgetragen.

Schlussfolgerungen:
Die retrospektive Analyse aller BOT-Fälle von Januar 1996 bis März 2011 in der Klinik für Frauenheilkunde und Geburtshilfe am Universitätsklinikum Jena zeigte, dass die Laparoskopie sowohl für die fertilitätserhaltende Therapie als auch für die radikale Therapie im Hinblick auf die untersuchten Parameter gleichermaßen sicher und effektiv ist wie die offene OP-Methode der Laparotomie. In unserem Patientinkollektiv mit sehr langem Follow up (median 98 Monate) hatte der operative Zugangsweg keinen Einfluss auf die Rezidivhäufigkeit. Die Patientinnen in der Gruppe der Laparoskopie hatten einen statistisch signifikant kürzeren Kliniksaufenthalt. Die fertilitätserhaltende Therapie erscheint bei jungen Frauen mit BOT eine Therapieoption

darzustellen; allerdings ist das erhöhte Rezidivrisiko mit dem Risiko von invasiven Implantaten zu berücksichtigen. Nach Abschluss der Familienplanung könnte eine Komplettierungsoperation das krankheitsfreie Überleben verlängern. Größere prospektive, multizentrische Datenerhebungen, wie die laufende ROBOT-Studie (AGO-OVAR OP.5), könnten diese Annahme weiter unterstützen.

1. Summary

Introduction: Based on 15 years of cumulative experience in laparoscopic treatment of borderline ovarian tumours (BOT) at the Jena University Hospital, we have observed operative outcomes, relapse-free and overall survival and complications related to the surgical approach. Fertility sparing surgery of women in reproductive age revealed as an appropriate treatment option in the management of BOT. To date, all trials examining laparoscopic surgery of BOT have been relatively small; therefore we focused our study on validating the feasibility and safety of laparoscopic surgery.

Patients and Methods: Between January 1996 to March 2011, we reviewed according to a prospective plan, the medical records of 45 patients diagnosed with BOT and treated them with laparoscopic surgery. In addition, we treated 15 patients with laparotomy in our hospital. Follow-up data were collected by telephone interviews with patients or their outpatient gynecologists. Laparoscopic staging was comprehensively performed in a standardized manner. We used the 1987 International Federation of Gynecology and Obstetrics classification (FIGO) for staging classification.

Thirty one patients underwent radical treatment and 16 patients underwent a fertility-sparing surgery. Parameters such as tumor diameter, histological type, CA 125 levels, operating time, length of hospital stay, complications, and recurrence were evaluated. Outcomes from patients who underwent fertility sparing surgery were compared with outcomes from patients with radical surgery, defined as hysterectomy, bilateral salpingo-oopherectomy and infracolic omentectomy. The inclusion criteria for fertility sparing surgery group was the preservation of the uterus and ovarian tissue in one or both adnexa.

Results: The patients' mean age was 47 years (16-78), mean diameter of the tumors was 60 mm (40-140mm) and mean CA 125 value was 31.8 (3.9-332U/ml). Mean follow up time or period was 83 months (median 98 months). Nine conversions to laparotomy were done, 3 cases due to assessment of malignancy, 1 due to tumor volume, 3 due to intraoperative diagnosis of FIGO III stage, 1 due to adhesions and 1 case because of a complication. Although the overall survival rate was 95%, tumor recurrence has been diagnosed in 7

patients (11.6%). There was no difference between laparoscopy and laparotomy regarding disease-free and overall survival. No major complications occurred when patients were treated by laparoscopy. A total of 16 patients underwent a fertility-sparing surgery (13 laparoscopically, 3 laparotomically). Three recurrences occurred in patients treated with radical surgery. 4 cases of recurrence were diagnosed in the conservative surgery group. The recurrence risk in conservative surgery group was twice as high as in radical surgery group (p= 0,42; Fisher exact test). However, no difference has been observed between laparoscopy and laparotomy group regarding recurrence risk. Pregnancy outcomes comprised 4 full-term deliveries.

Conclusion: The use of laparoscopic surgery still remains controversial due to accuracy of staging, intraabdominal tumor rupture and port site metastasis. Fertility sparing surgery of women in reproductive age can be an appropriate treatment option in management of BOT. However, for women who passed reproductive age or do not desire having more children, a second look surgery or radical treatment is recommended. Our study confirms that laparoscopic surgery is a safe and effective method in the management of BOT

2. Introduction

2.1. Borderline Ovarian Tumors (BOT) from the historical point of view.

Borderline ovarian tumors (BOT) have been first described by Taylor in 1929 as “semi-malignant” tumors of the ovary (Taylor, 1929). The concept of BOT has been officially accepted in 1971 by the International Federation of Obstetrics and Gynecology and two years later also by WHO (Serov et al., 1973). In the current WHO classification there is a unique definition for BOTs “tumours of low malign potential” (LMP) (Scully, 1999). In the literature there is no consensus concerning the definition of BOT. BOTs are characterized by a degree of cellular proliferation and nuclear atypia in the absence of infiltrative destructive growth or obvious stromal invasion (Tinelli et al., 2007). Despite its tendency to become malignant tumors, BOT has a good prognosis. Today, many authors postulate criterion to distinguish between benign and malignant BOT (Seidman et al., 2002). Others found previous classification of FIGO and WHO to be more useful.

2.2. Definition of BOT

Borderline tumors are clinically and morphologically classified between benign (cystadenomas) and malignant tumors of the epithelial ovarian tumors. The definition of BOT includes ovarian tumors with nuclear atypia, mitotic activity, formation of papillae, and without stromal invasion. Extraovarian lesions with invasive growth can infrequently occur (Bell et al., 1988; Gershenson and Silva, 1990; Gershenson et al., 1998a; Gershenson et al., 1998b; McCaughey et al., 1984; Michael and Roth, 1986). In rare cases, a lymphogenic or hamatogenic spread can also be observed (Seidman and Kurman, 2000). BOTs have been similarly described as invasive and benign ovarian tumors. Histologically, serous, mucinous, endometrioid, clear cell tumors could be differentiated among all types. Despite favorable prognosis of most borderline tumors, its pathological behavior is different from benign lesions of the same cell type (cystadenomas, adenofibroma). The term “atypical proliferating tumor” should therefore not be used due to the few borderline tumors that have a malignant potential.

2.3. Incidence and etiology of BOT

Borderline tumors represent approximately 8% of all epithelial ovarian tumors and about 32% ovarian cancers (Katsube et al., 1982). Their incidence is 1.8 to 4.8 / 100,000 women per year (Katsube et al., 1982; Auranen et al., 1996; Björge et al., 1997; Harlow et al., 1987). However, the age-adjusted incidence appears to have increased in recent decades for women in the reproductive age (Björge et al., 1997; Harlow et al., 1987). The peak age of incidence of borderline tumors is about 40-52 years (Auranen et al., 1996; Harris et al., 1992, Trimble C. and Trimble E. 1994) which is at least 10 years earlier than the ovarian cancer (Auranen et al., 1996; Harris et al., 1992). The recent reports show the increase of incidence of BOT, especially a relative increase in the proportion of the BOT compared to other ovarial malignancies.

In the USA, a slight decrease in the incidence of invasive cancers in the second Half of the 90s with a constant incidence of BOT has been observed (Mink et al., 2002). In Sweden, the incidence has risen since 1960 from 1.0 to 5.3 in 2005, while the incidence of invasive cancer has fallen slightly since 2000. In Israel, the incidence rose from 0.83 in the years 1985-89 to 1.54 per 100,000 women in the years 1990-1993 (Iscovich, 1998). An increase in the incidence of 1.7 to 2.7 from 1976 to 1981 compared with 1987-1991 has also been reported in Switzerland (Levi et al., 2002). The FIGO Annual World Report demonstrated the distribution of BOT and invasive carcinoma of the BOT to a relative increase since the late 80s (Heintz et al., 2006).

Pathological diagnosis is a prerequisite for identification of histological features of BOT and prediction of good or poor prognosis. It has long been held that borderline tumors were precursors of invasive ovarian cancer. However, this approach has been questioned, as both epidemiological and molecular biological studies produce evidence of distinct differences between these two groups of tumors. Borderline ovarian tumors often occur in reproductive-age women. Because of the generally benign behavior of these tumors, their management has become progressively more conservative, allowing women to maintain their fertility (Crispens, 2003).

Many risk factors have been described to be involved in the pathogenesis of BOT. Epigenetic mutations in the BRCA loci have been reported by other authors. However, these mutations are not associated with poor diagnosis of

BOT (Pal et al., 2005; Gotlieb et al., 2005). In contrast, smoking seems to be a potent risk factor for BOT in rare mucinous carcinomas, except for invasive ovarian carcinoma (Gramm et al., 2008; Jordan et al., 2007). An increase in smoking among women in the 1980s may be associated with an increase of the relative frequency of BOT.

Potential risk factors for invasive ovarian cancer are linked to various reproductive factors. A relative decrease in the incidence of invasive cancers is associated with increasing duration of oral contraceptives. A significant reduction in risk was found in the common subtype of ovarian carcinoma of serous type. The other reproductive factor that was associated with an increased risk for BOT (and invasive carcinoma) is infertility (Zreik et al., 2008; Rossing et al., 2004; Cetin et al., 2008). The reports for treatment with clomiphene in order to stimulate the ovulation and the use of other drugs in the fertility treatment do not provide consistent results.

The result of a meta-analysis including more than 54,000 patients and more than 20,000 IVF patients showed no increased risk of BOT for fertility gonadotropin, HCG, GnRH analogues and clomiphene, and no increase in the risk of breast and ovarian cancer, with the exception of endometrial cancer (Jensen et al., 2009). Considering the prognosis of the BOT and the coincidence of the BOT with infertility, it is difficult to generate valid data. In addition, Riman et al. (2001) evaluated the risk factors for borderline ovarian tumors in a nationwide, case–control study. They found that parous women had a reduced risk of developing borderline tumors compared with nulliparous women [odds ratio (OR) 0.44 for serous tumors and 0.63 for mucinous tumors]. They also found the lactation to be protective. Similar findings have been observed in invasive ovarian cancer. On the other hand, unlike in invasive ovarian cancer, oral contraceptive use was not protective against the development of borderline tumors (OR 1.4).

2.4 Histology & Tumor Staging

The BOT are similarly termed like the invasive and the benign ovarian tumors: serous, mucinous, endometrioid, clear cell or transitional cell, the two most common types - mucinous and serous borderline tumors. In a German retrospective review with a total of 5808 patients, the proportion of serous BOT was 53.3% and mucinous BOT 42,5 % (du Bois et al., 2009). The proportion of mucinous tumors in BOT differs significantly from the ovarian cancer. In ovarian cancer the mucinous type occurs at a frequency of <10 %. Mucinous BOTs are classified as either intestinal (85%) or endocervical/Mullerian-type (15%) depending on the nature of the lining. In 10% of cases mucinous BOTs are associated with pseudomyxoma peritonei and may then be derived from the gastrointestinal tract, mostly the appendix (Scully et al., 1999). The BOT has the same FIGO classification as the invasive ovarian cancer. The distribution of staging differs in two diseases. FIGO Stage I, tumor diagnosed as limited to the ovaries, can be observed in invasive carcinoma only about 25%. In BOT the proportion of the stage FIGO I is about 75% (Sherman et al., 2004).

2.5 Clinical findings prior to diagnosis

There are no specific symptoms in BOT compared to ovarian cancer. In general, the increase of abdominal circumference (20-92%), abdominal pain (10-58%), bleeding disorders (6-44%) and disorders of bowel and bladder function (5-13%) have been reported. Up to 30% of all cases are incidental findings in asymptomatic women (Hoskins, 1995). For the preoperative diagnosis the bimanual palpation, ultrasound findings and serum CA125 levels can be helpful but none of them represent a reliable and specific method. A study of BOT showed the sensitivity of ultrasound 87% and the sensitivity of CA 125 levels 62% (Gotlieb et al., 2000). For the intraoperative diagnosis a frozen section can be done but the validity of a diagnosis from the intraoperative frozen section is

significantly lower than in ovarian carcinomas (Medeiros et al., 2005; Geomini et a., 2005; Atallah et al., 2004).

2.6 Therapy

2.6.1 Operative Staging

For women with borderline ovarian tumors, the optimal surgical removal of the tumors is the most important aspect of the treatment and it may reduce the risk of recurrence (Cadron, 2007). The removal of the ovaries, fallopian tubes, uterus and omentum, peritoneal washings and complete peritoneal resection of macroscopic lesions, and multiple peritoneal biopsies in case of absence of over peritonelcarcinosis is usually performed as state of the art surgery, occasionally termed *radical surgery*. In addition, appendectomy should be performed in mucinous BOT to exclude the possibility of ovarian metastasis of a mucinous tumor of the appendix (Schmalfeldt et al., 2007). Lymphnode(s) staging is no longer recommended. It does not appear as a prognosis factor for advanced-stage BOT because lymphnode(s) positivity is not associated with the recurrence (Lesieur et al., 2010).

2.6.2 Conservative or radical surgery

The prognostic value of a complete staging in BOT differs from ovarian cancer where it is mandatory. When the diagnosis of BOT is made, patients and gynecologists are confronted with choosing conservative or radical surgery. Conservative surgery is defined as a surgery preserving the uterus and at least a part of one ovary. This management was safe not only in patients with early-stage BOTs but also in patients with advanced-stage BOTs with noninvasive extraovarian implants, if these implants could be resected completely (Nam,

2010). After a conservative management the rate of recurrence was higher but without an impact on survival. The most recurrent lesions are borderline tumors and located in the remaining ovary (Morice 2006, Nam 2010).

2.6.3 Prognosis of BOT

The prognosis of borderline tumors is favorable in the vast majority of cases. Recurrences were detectable with few exceptions only if tumor was bilateral or extraovarian primary tumor manifestations were seen (Kaern et al., 1993). At least 90% of patients survive after 10 years from the day of diagnosis (Trope et a., 2000). Generally accepted prognostic factors are tumor stage (FIGO I versus II / III, Ren et al., 2008; Lenhard et al., 2009; du Bois et al., 2009) postoperative residual tumor (yes versus no; Kaern et al., 1993; Trope et a., 2000; Bell et al., 1988), histological type (serous-muzinous versus others; Kaern et al., 1993) and age (≤ 70 years versus> 70 years; Kaern et al., 1993). The advanced FIGO stages II-IV are defined by extraovarian involvement. In particular, peritoneal implants play important role for the prognosis of BOT. They are classified into non-invasive and invasive implants, which may have different prognostic significance (Seidmann et al., 2002). Invasive implants have been proven to be an important prognostic factor for borderline tumors of the serous membranes (Seidmann et a., 2002). The so-called micropapillary serous BOT subtype could also be considered as prognostic factor regarding tumor biology. Some authors found significantly worse prognosis in micropapillary BOT prognosis (Silva et al., 2006) and some authors have observed only a statistical trend (Chang et al., 2008). The impact of microinvasion on prognosis of BOT has been reported in the largest published single series to be statistically significant (Cusido et al., 2007; Ren et al., 2008; Buttin et al., 2002).

2.7. Laparoscopy

2.7.1 Laparoscopic management of ovarian tumors and BOT

Laparoscopic treatment of adnexal masses has been shown to be a safe and effective diagnostic and therapeutic tool in the hands of experienced laparoscopists (Seracchioli et al., 2001). The laparoscopic approach for therapy of BOT is still under debate as well as in early invasive cancer of the ovary. On the other hand, laparoscopy seems to be an attractive approach for BOT as it is for benign tumors of the ovary (Fauvet et al., 2005, Odegaard et al., 2007). Laparoscopic surgery increases the chances of subsequent pregnancy (Romagnolo et al., 2006), possibly because fewer adhesions form within the pelvis. Recovery from laparoscopy is also faster, which leads to a shorter hospital stay (Odegaard et al., 2007). Moreover, the possibility to oversee invasive implants in the abdomen has been suspected and the risk of rupture of the BOT cyst has been reported to be higher in several retrospective studies (Fauvet et al. 2005). The oncologic meaning of these iatrogenic ruptures is unclear.

3. Aims of the study

1. Retrospective analysis of clinical results obtained after laparoscopic treatment of BOT at the Jena University Hospital.

2. Comparison of the laparoscopic surgery for BOT with laparotomy regarding clinical and oncological outcomes at the Jena University Hospital.

3. Oncological prognosis in terms of disease-free survival and overall survival of patients who underwent laparoscopic surgery for the operative staging for BOT.

4. Outcome of fertility preservation of BOT patients with respect to pregnancy rate and the oncological safety.

4. Patients and Methods

4.1 Patients

Medical records of 60 patients with borderline ovarian tumors (BOT) managed surgically from January 1996 to March 2011 were collected from gynecologic oncology and pathology files at the department of Gynecology, Jena University Hospital, Germany.

While 50 patients were treated initially with complete surgery for the ovarian tumor and peritoneal disease at the Jena University Hospital, 10 patients were referred to us from other hospitals following incomplete surgery (performed by laparoscopy or laparotomy).

Thirty-one of sixty patients underwent surgery once and 29 received a second surgery for an operative completion.

The following parameters were registered from each case: age at primary diagnosis, menopausal stage, tumor size, CA 125 levels, surgical procedures performed, tumor type, tumor stage, duration of surgery and hospitalization, intraoperative and postoperative complications. In the follow up data, the occurrence of relapse, time to relapse, survival and pregnancy rates in fertility sparing surgery cases were registered. These detailed informations were reviewed from the medical reports and contact with patients or their gynecologists. No patient was lost to follow up.

Histological types and stages were recorded by using the macroscopic descriptions during the surgical procedure and by reviewing pathology records according to the 1987 FIGO classification (Bell et al., 1988). All patients underwent transvaginal ultrasound.

4.2 Methods

As standard method, carbondioxide was used with an intraabdominal pressure of 12-13 mm Hg in all laparoscopic surgeries. A pneumoperitoneum was established by using a Veres needle. A 10 mm trocar was inserted through a 1 cm skin subumbilical incision and three suprapubic ancillary trocars were used: one 5-mm trocar was inserted in the midline 3 cm cranial to the symphysis, and one in each laterally to the inferior epigastric vessels for meticulous inspection

of the pelvis and the abdominal cavity. Samples of free peritoneal fluid were obtained. In case the the fluid was absent, a peritoneal washing with saline solution was performed and drained for cytological analysis.
Laparoscopically removed tissues from abdominal cavity were collected in a plastic bag intra-abdominally.
Frozen section preparation was carried out in 35 patients (58,5 %). The 45 patients who underwent laparoscopic surgery (as a primary surgery or after an incompleted surgery) were compared with 15 patients who had a surgery by laparotomic approach.
The conservative surgery was defined as preservation of the uterus and at least one ovary. The radical surgery was defined as hysterectomy with a bilateral salpingo-oophorectomy, infracolic omentectomy, peritoneal biopsies and systematic appendectomy (for mucinous borderline tumors). If there were no obvious abdominal or pelvic peritoneal lesions, peritoneal biopsies were performed. Lymphnode(s) sampling from pelvic or paraaortic regions was performed in some cases until 2005.
Patients were examined either in our clinic or by their gynecologist at 3-month intervals after initial diagnosis for a 2-year period and at 6-month intervals for an additional 2 year period. Further, a yearly sonographic evaluation was performed to detect the clinical signs of recurrence. The progress of the disease was monitored in 40 patients over more than five years and in 15 patients, over a period of more than 10 years. The survival rates after five and ten years (depending on the stage) were calculated. Various parameters such as age, tumor size, tumor markers, iatrogenic tumor rupture, duration of surgery, and hospital stay were analyzed statistically.

4.3 Statistics

For the statistical analysis we used the SPSS software (version 19.0, Windows). The impact of radical and conservative treatments of laparoscopic and laparotomic approach, with survival and recurrence rates was tested using Fisher's exact test for small or very small cohorts. The chi-square test was used to compare two samples characterized by a qualitative event (eg, tumor rupture yes / no). Differences between mean values were analyzed using

the Student`s t test with two-tailed P values. The cut-off for statistical significance was set at $P < 0.05$.

5. Results

5.1. Patients characteristics

A total 60 patients with BOT were included in our study. The mean age of the patients at the time of the diagnosis was 47 (ranging from 16 to 78 years). Mean Follow up time was 83 months (minimum 1, maximum 200 median 98 months). Thirty-two women (53 %) were premenopausal. Histology revealed serous tumor subtype in 46 women (77 %), mucinous in 8 (13 %), Brenner tumor in 1 (2 %), granulosa cell tumor in 5 (8 %). Thirty-three patients (33,55%) diagnosed in Stage Ia, 7 in Stage Ib (7,12 %), 14 Ic (14,23%), 1 stage IIIb (1,2%), 5 stage IIIc (5,8 %) (**Table 1; Figure 1**). In these 6 stage III cases, peritoneal implants were non-invasive. Cytology was positive for tumor cells in 8 cases (24%, 8/33). The localizations of the implants in 6 cases were the peritoneum and colon. One patient had previous history of BOT and was characterized as recurrent disease, 120 months after the initial BOT.

Table 1. Histology and FIGO staging of BOT

		Staging					Total
		Ia	Ib	Ic	IIIb	IIIc	
Histology	Brenner	1	0	0	0	0	1
	Granulosa	4	0	1	0	0	5
	Mucinous	7	0	1	0	0	8
	Serous	21	7	12	1	5	46
Total		33	7	14	1	5	60

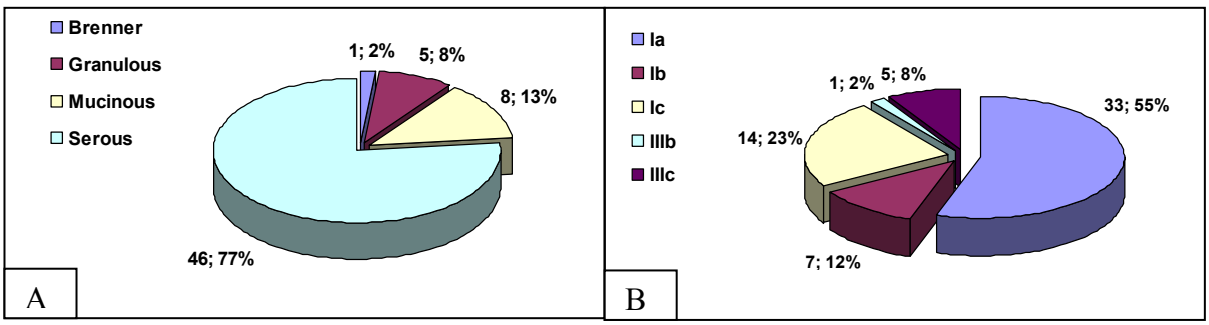

Figure 1. Histological types of BOT (A) and FIGO staging (B)

- **Frozen sections**

In order to determine the accuracy of histological diagnosis based on frozen sections, we examined BOT cases analyzed with frozen sections. Perioperative frozen section histology was evaluated in 35 patients out of 60 patients with BOT. When compared with the final histology, 8 of those with borderline tumors (22 %) were incorrectly diagnosed as benign: Two of 5 mucinous borderline tumors were classified as benign, and 5 serous borderline tumors of 27 frozen sections were considered benign. In one case of a granulosa cell tumor with low malignant potential the frozen section was incorrectly diagnosed as benign.

- **Tumor marker**

There was a significant correlation between tumor size and CA125 value (p value <0.001; Pearson correlation test) **(Figure 2).** The rate of the patients with increased CA 125 levels (>35 IU/l) in the group of stage III patients was significantly higher than the group of stage I (p value: 0,023, fisher exact test). CA 125 was positive in 23 of 45 patients with serous BOT (51.2 %). We had 8 patients with mucinos BOT. There was no CA 125 positivity in the patients with mucinous BOT. **(Table 2).**

Table 2. Association between tumor marker, histological type and staging

Histological type	**CA 125** (mean value)	**Increased** (>35)
Serous (n= 45)	120	n=23
Mucinos (n=8)	26,80	n=0
Granulosa Tumor (n=5)	18,83	n=0
Brenner (n=1)	70	n=1
Total (n=60)	100,30	n=24
Stage	**CA 125** (mean value)	**Increased** (>35)
Ia	45,88 (n=27/33)	n=9
Ib	86,17 (n=7/7)	n=4
Ic	213,33 (n=12/44)	n=7
IIIb	44 (n=1/1)	n=1
IIIc	168,8 (n=4/5)	n=5

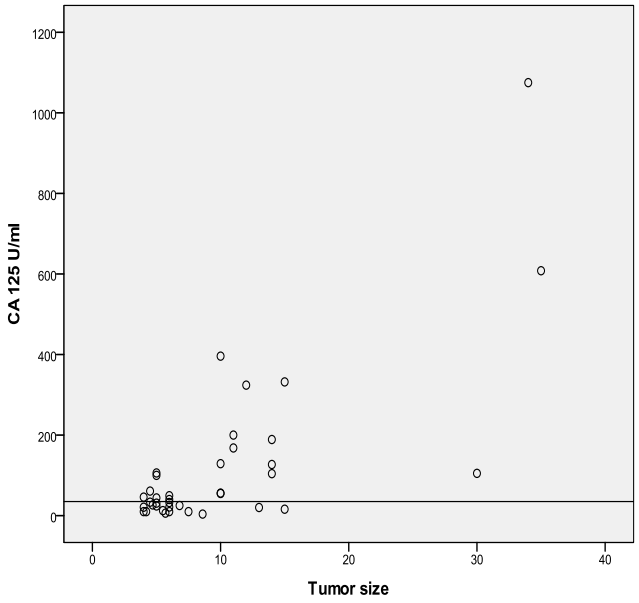

Figure 2. Correlation diagramm of tumor size and CA 125 levels

5.2 Operative procedures: Laparoscopy vs. laparotomy

38 patients underwent laparoscopy and 22 underwent laparotomy at the primary surgery. 29 patients received second surgery for the operative completion. Therefore, 26 patients received a laparoscopy and 3 patients had a laparotomy. In total, 29 women were treated by conservative organ preserving surgery. Average diameter of the cyst and CA 125 levels were significantly higher in patients treated by laparotomy at the primary surgery compared to the laparoscopy group. **(Table 3a).**

Table 3a. Primary Surgery. Laparoscopy vs. laparotomy

Primary Surgery			
	Laparoscopy n=38	Laparotomy n=22	P-Value
Age (years)			
Mean	48	45	0.61
Median	49	45.5	
Range	18-78	16-45	
Tumor size (cm)			
< 10 cm	32	6	
>10 cm	6	18	
Mean	6.62	18.05	<0.001
Median	6	18	
Range	3-14	5-40	
Intraoperative cyst rupture	8	3	0,732 *
CA 125 levels	34	17	
Mean	50.35	200.18	0.04**
Median	27.1	105	
Range	3,9-396	10-1075	

*Pearson Chi-Ouadrat test ** Mann-Whitney-U test

Laparoscopic surgery was performed in 45 cases (first surgery and/or completion surgery). The conversion from laparoscopy to laparotomy was performed in 9 cases: three cases due to macroscopic suspicion of malignancy, 1 due to a large tumor volume, 3 due to FIGO III staging, 1 due to massive adhesions and 1 case due to a bleeding complication. Thirty-one women (51.6 %) underwent radical surgery, 20 (64.5 %) laparoscopic procedures, 11 (35.4%) laparotomic procedures.

Tissue samples were removed from the abdominal cavity using a plastic bag by laparoscopic procedures to reduce the risk of peritoneal spillage or the parietal implantation of neoplastic cells.

In 11 of 60 patients (18.3 %), tumor rupture or spilling during surgery occurred. The incidence of the intraoperative rupture was not significantly higher in the group of patients treated by laparoscopy compared to the group treated by laparotomy (laparoscopy:8, laparotomy:3; p value: 0.732).

Five patients had a cystectomy of the ovarian cyst, 14 unilateral adnexectomy, 40 bilateral adnexectomy, 11 contralateral biopsy and 37 hysterectomy. Omentectomy was performed in 45 patients and appendectomy in 26 patients. (Figure3).

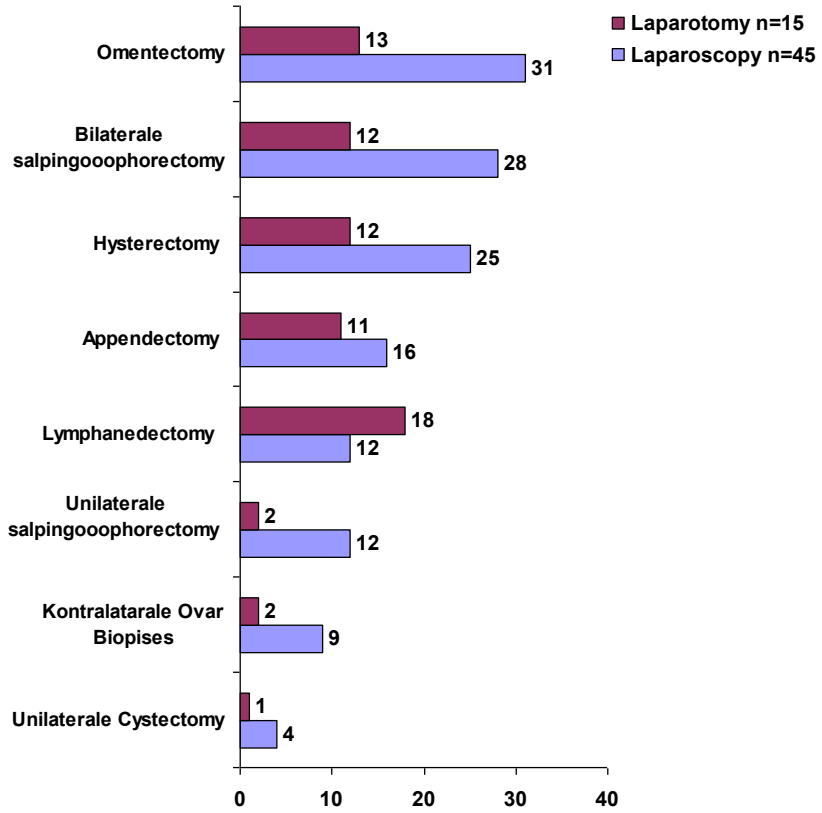

Figure 3. Operative procedures in management of BOT

We examined the surgical methods of the patients who had a conservative management regarding to the recurrences. We found 5 Patients with a cystectomy and 24 with oophorectomy. The risk of tumor rupture in cystectomy group was higher but the difference compared to the patients with oopherectomy was not significant. No patient with cystectomy had a recurrence. (Table 3b)

Table 3b. Procedures for the conservative management of BOT

	Cystectomy (n=5)	Oopherectomy (n=24)	P value
Tumor rupture	2 (40%)	7 (29.2%)	0.385
Recurrence	0	4 (16.6%)	0.447

We have also compared the results of two different surgical approaches. In the laparoscopic surgery group both the average hospital stay ($p < 0.001$) and the duration of surgery ($p = 0.037$) were significantly shorter **(Table 4).**

Table 4. Hospital stay: Laparoscopy vs. laparotomy

OP approach	Laparoscopy	Laparotomy	P Value
Duration (min) Mean Median	n=42 183.5 176.5	n=13 241.4 230	0.037
Hospital stay (days) Mean Median	n=42 8.1 7	N=15 15.2 14	< 0.001

Lymphonodenectomy was performed in 30 cases (18 laparoscopically, 12 laparotomically). There was no statistically significant difference of the number of lymphnodes removed between laparotomy and laparoscopy groups **(Table 5).**

Table 5. The comparison between numbers of lymphnodes removed during laparoscopy and laparotomy

	Laparoscopy (n=15*/45)	Laparotomy (n=11*/15)	p value
Lymphnodes removed (mean value)	22.47	22.45	0.567

*cases of which the number of Lymphnodes removed was known

The duration of surgery was similar if the lymphonodectomy was done with laparoscopy or with laparotomy and the hospital stay in the former case was significantly shorter than the latter group (p: 0.02) (Table 6).

Table 6. Duration of the surgery and hospital stay in cases with lymphonodectomy

OP approach	Laparoscopy	Laparotomy	P value
Duration of the surgery (min) Mean value	n=16 241.88	n=10 270.60	0.481
Hospital stay (days) Mean value	n=15 10.33	n=12 16.33	0.02

5.3 Recurrence of BOT

Of note, 7 out of 60 patients (11.6%) had a recurrence of BOT disease. The patients were between the age of 29 and 70 (average 49.5). Serous tumor was found in all of patients with recurrence. In patients with recurrence, there was no increase of CA125 levels except for one patient (CA 125 was 100 U/ml). Follow-up analysis showed recurrence after 76.8 months (mean value; 22-120 months, median 84 months). Out of 7 relapse cases 4 cases developed again a BOT and in 3 an invasive ovarian cancer. Detailed information concerning recurrence of BOT is presented in Table 7. After an effective treatment of the first relapse of BOT, none of the four patients had a secondary relapse.

Table 7. Patients with recurrence disease of BOT

	Age	Staging	Histology	CA 125 (U/l)	TU Size (cm)	Procedure	OP approach	Time to first recurrence	Final procedure / Type of recurrence *	Follow up after recurrence *
1	70	Ia	Serous	21.4	6	AE uni	LSK	84	LSK, HE, AE li LNE pe, pa, Om BOT	+ 74
2	58	IIIc	Serous	100	5	HE+ AE bil+ App+LNE pe, pa + Om	LSK →Lap	73	Lap, Debulking, Ovarian CA	+ 9
3	39	Ia	Serous	33.4	4,5	AE uni	LSK	100	LSK→ Lap, Debulking Ovarian CA	+ 30
4	51	Ib	Serous	31	5	AE uni	LSK	22	Lap, Debulking, Ovarian CA	Died after 24 months
5	39	IIIc	Serous			AE bil+ HE + Om	Lap	120	Lap, Debulking BOT	+ 80
6	29	IIIb	Serous	44	5	AE uni+ Ovar Biopsy contr. App + Om + LNE pe, pa	Lap	41	Lap, AE re BOT	+124
7	61	Ib	Serous	10	7	AE bil+HE+ LNE pe, + Om + App	LSK→Lap	98	Lap, Debulking BOT	+4

AE: Adnexectomy, **HE:** Hysterectomy, **Om:** Omentectomy, **LNE**: Lymphonodectomy, **App:** Appendectomy, **uni:** unilateral, **bil:** bilateral, **pe**: pelvic, **pa**: paraaortic
LSK: Laparoscopy, **Lap:** Laparotomy
* months

First patient with recurrence of BOT disease was 70 years old at the time of initial diagnosis. A laparoscopic unilateral adnexectomy was performed due to the tumor size (6 cm) on the right side. The level of CA 125 was analysed as 21.4 U/ml. After 84 months this woman developed a solid cystic tumor on the left ovary. Therefore, a complete laparoscopic staging was carried out (hysterectomy, adnexectomy, omentectomy, pelvic and paraaortic lymphonodectomy).

The 58 year old second patient had a laparoscopic adnexectomy, because of large ovarian cysts of 5 cm on both sides. The both ovaries displayed micropapillary pattern. The level of CA 125 was 100 U/ml. The patient was treated by laparotomy with hysterectomy, infragastric omentectomy, peritoneal biopsies and pelvic and para-aortic lymphadenectomy. The BOT was found in frozen section. The cytological examination showed positive tumor cells at primary surgery (Pap V). A recurrence behind the vagina has been diagnosed after 73 months. Histology showed a serous papillary invasive ovarian cancer (tumor staging IIIc). We treated the patient with 6 cycles of paclitaxel and carboplatin chemotherapy.

The third patient was 39 years old and had previous laparoscopic unilateral adnexectomy. The tumor was approximately 4.5 cm in size and CA 125 level was 33.4 U/ml. We observed a 10 cm cystic recurrence on the other ovary after 100 months. A laparoscopic cystectomy was performed without a rupture. Frozen section showed a serous invasive ovarian cancer. In this same session, we performed a debulking laparotomy according to the guidelines. The stage of the tumor was Ic. After 6 cycles of chemotherapy with carboplatin and taxol no recurrence has been observed since 30 months.

The fourth patient was 51 years of age and postmenopausal at the time of first diagnosis. Tumor marker CA 125 was analysed as 31 U/ml. The ovarian tumors on both sides were detected with ultrasonography (left: 3 cm, right: 6 cm). A bilateral laparoscopic adnexectomy was performed. Severe intra-abdominal ascites was reported after 22 months. CA 125 was 86U/ml. The advanced ovarian cancer required a radical debulking surgery including pelvic as well as para-aortic lymphadenectomy by laparotomy. Subsequently, the patient received chemotherapy with six cycles of carboplatin and paclitaxel. 24 months after diagnosis of recurrence the patient died.

Another 39 years old patient with recurrence of BOT was operated by laparotomy.The frozen section of a unilateral adnexectomy was positive for BOT disease. Due to this fact we extended the operation and carried out an adnexectomy on the other side, and a hysterectomy with omentectomy and peritoneal biopsies. A recurrence between the vagina and rectum was observed 120 months after the first diagnosis. The recurrence was histologically confirmed by a frozen section examination at a diagnostic laparoscopy. A re-laparotomy with debulking surgery was performed. Eighthy months after diagnosis recurrence was not present.

The sixth patient was 29 years old and nulliparous. She wished a fertility-preserving procedure. CA 125 was 44 U/ml. Solid cystic enlarged ovaries (on both sides about 5cm) were identified using sonography. We performed an adnexectomy left with partial excision of the right ovary and an omentectomy, appendectomy and a lymphadenectomy (pelvic and para-aortic) using laparotomy. Twenty four lymph nodes were removed and all of them were free of tumor. On the liver capsule, there were small macroscopically detectable non-invasive implants (< 2cm; staging IIIb). We identified a recurrence on the right ovary after 24 months by a routine examination and performed a partial resection of this ovary laparotomically. Twenty seven months after the first recurrence the patient underwent a laparoscopic right adnexectomy for a new recurrence.

The seventh patient was 61 years of age at the first diagnosis. She had an ovarian tumor of 7 cm. The CA125 level was 10 U/ml. Medical history revealed that the patient had undergone hysterectomy several years ago. We performed a diagnostic laparoscopy followed by a conversion to a laparotomy for a complete staging. A bilateral adnexectomy, omentectomy, lymphonodectomy (pelvic and paraaortic) was carried out. Tumor staging was determined postoperative as pT1b. We observed a recurrence of the disease in the pelvis with ultrasound after 98 months from the first surgery. The CA 125 level was 39 U/ml. A diagnostic laparoscopy with a conversion to laparotomy for a debulking surgery was performed. The patient continued to live without any other new recurrence or new symptoms 4 months after this first recurrence.

The risk of recurrence of BOT in stage Ia was significantly lower as compared with other histological stages (p value = 0.046). In stage IIIc, the risk of recurrence was 10.33 fold increased when compared with stage Ia. Recurrences were identified in 16.7% of patients who underwent a conservative surgery. Less cases of recurrence were found (6.7%) when patients were operated completely. Despite approximately 3 times more relapses, there was no significant difference between these two groups. **(Table 8).**

Table 8. Recurrence rates in relation to surgical treatments.

Complete Staging*	Recurrence		Total	P value (Fisher Exact Test)
	Yes	No		
Yes	n=2 6.7 %	n= 28 93.3%	n=30 100%	0.424
No	N= 5 16.7%	N=25 83.3%	n=30 100%	

*Hysterectomy, bilaterale adnexectomy, omentectomy, peritoneal biopsies and washings

5.4 Survival

From a total of 60 patients 7 patients have had a relapse. Three recurrences were histologically ovarian cancer and 4 of the 7 were ovarian BOT again. Six of 7 patients who developed a recurrence were still alive without a new recurrence at the time of this study. There were 3 deaths. One patient died 24 months after the diagnosis of the recurrence of ovarian cancer. One patient died of lung cancer and one died of colon cancer. Disease-spesific survival rate is 98,3% and the overall survival rate is 95%. Recurrence-free survival rate is 88.3% **(Figure 4)**. In terms of relapse-free survival there is no significant difference between the two surgical methods **(Table 9).**

Table 9. Recurrence of the disease: Laparoscopy vs. Laparotomy.

Method of surgery	Recurrence	Recurrence-free	P value
Laparoscopy (n=45)	n= 5 11.1%	n=40 88.9%	0.813
Laparotomy (n=15)	n=2 13.3%	n=13 88.3 %	

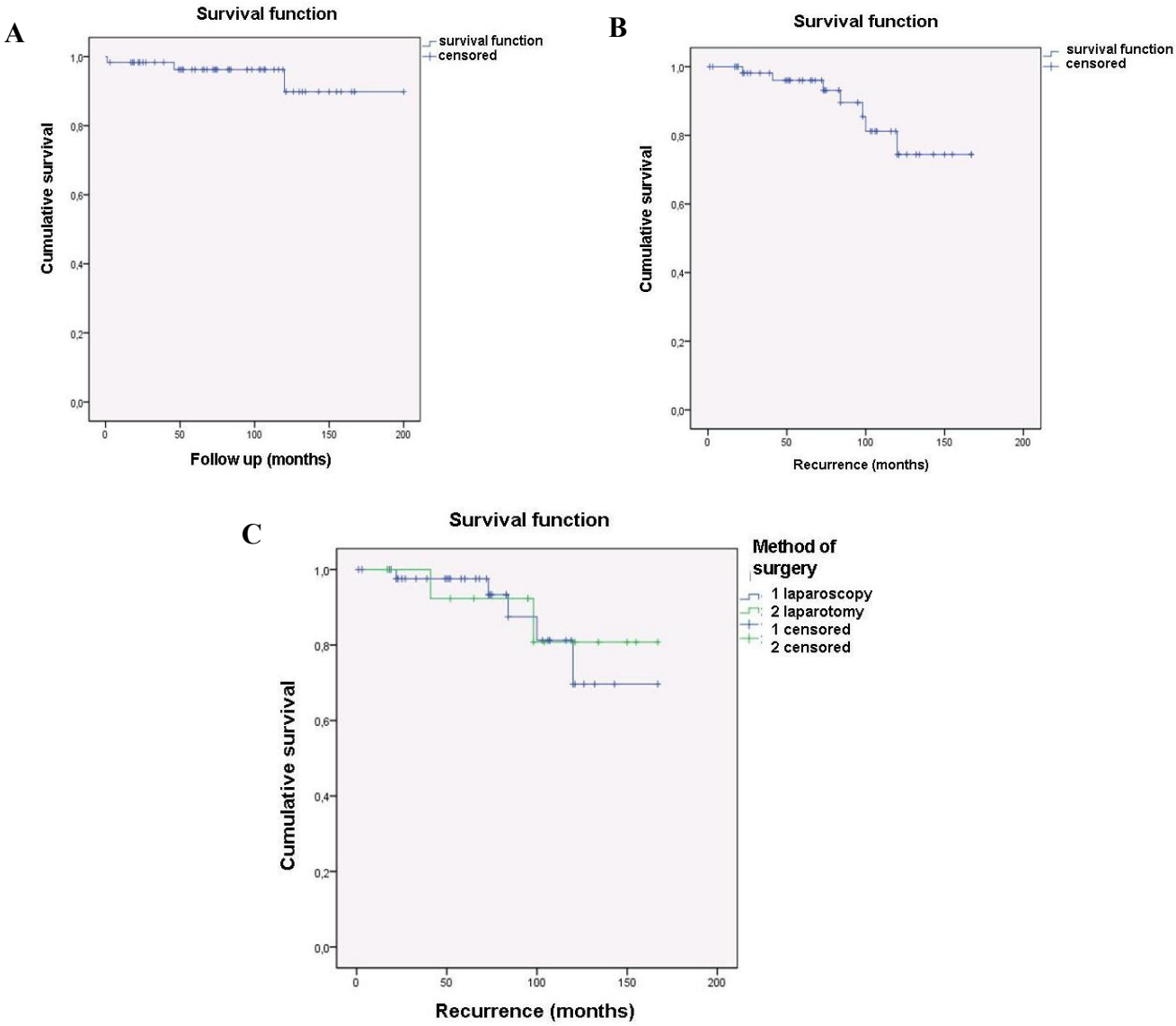

Figure 4. Kaplan –Meier analysis of follow up (A), recurrence (B) and recurrence considering the method of surgery (C).

5.5 Fertility sparing treatment and pregnancy outcomes

The criteria used to decide whether or not to perform fertility-sparing management were young age (<45 years), low parity (mostly nulliparous) and possibility of close follow-up. Moreover, the patient had to be compliant with frequent follow-up visits**.** In the group of 16 patients treated by fertility sparing surgery, 6 patients (25 %) preoperatively stated clearly to desire pregnancy subsequent to surgery. Four (25%) of these patients conceived spontaneously, resulting in a total of 4 pregnancies. All of them had a full term delivery and no fetal abnormalities were reported. Two of these six patients had a recurrence (1

BOT, 1 ovarian cancer). The other 10 remaining patients so far have no current desire for pregnancy and are free of disease.

5.6 Complications followed by surgery

There was no difference in complications comparing laparoscopic and laparotomic procedures.

Three perioperative complications and 3 postoperative late complications were documented in the laparoscopy group. In patients who underwent a laparotomy 3 perioperative complications und 5 late postoperative complications were detected **(Table 10-11).**

Table 10. Early complications: Laparoscopy vs. laparotomy

Early complications	Laparoscopy	Laparotomy
Bowel injury	2	0
Gastric injury	0	1
Great vessel injury and bleeding with a need of transfusion	1	2

Table 11. Late complications: Laparoscopy vs. laparotomy.

Late complications	Laparoscopy	Laparotomy
Postoperative infection in abdomen	1	0
Pulmonary embolism	1	0
Thrombosis	1	2
Postoperative Bleeding	0	1
Lymphocele as a focus of infection	0	2

6. Discussion

Borderline ovarian tumors, with low malignant potential, comprise 15% of all epithelial ovarian neoplasms (Ozoels et al., 1997). The outcome for women with borderline tumors is much better than for women with invasive ovarian cancer. However BOT affects a younger age group where future fertility is an important issue for many of these women. The performance of laparoscopic surgery for treatment of BOT still remains controversial due to inaccuracy of staging, intraabdominal tumor rupture and port site metastasis. Based on our 15 years of observation and experience in laparoscopic treatment of BOT, we aimed to describe the role of minimal invasive surgery for recurrence and survival compared to radical laparotomic surgical management. We also focused our study to validate the feasibility and safety of fertility sparing surgery and to investigate the pregnancy outcomes.

The peak age of incidence of borderline tumors is about 40-52 years which is at least 10 years earlier than the ovarian cancer (Harris et al. 1992, Auranen et al. 1996). FIGO I staging by BOT patients is more common than the occurance of such stage in invasive ovarian cancer (IOC) (Sherman et al, 2004). In our study, the average age of the patients was 47. Ninty percent of the patients were FIGO stage I. Stage III was found in 6 cases (10 %) and stage II and stage IV disease was not encountered.

In ovarian cancer and BOT serous cell type is dominant and comprises the majority of cases. Mucinous cell type is rarely seen in ovarian cancer (2.7%). In contrast, mucinous BOT occurs more often than invasive ovarian cancer (53.6%) (Hart WR 2005; Seidman et al., 2004; du Bois et al., 2009). In 60 patients, who we have examined retrospectively, there was 46 cases with serous BOT (77%) and 8 cases with mucinous BOT (13%).

There are some selected reports indicating significant correlation between serum CA 125 levels and tumor size (Gotlieb et al. 2000, Zanetta et al. 2001, Ayhan et al., 2007). In patients who had serous BOT with advanced stage, higher CA 125 levels than stage I has beed identified (Rice et al., 1992).

Also, we found a significant correlation between tumour size and CA125 levels (p value <0.001; Pearson correlation test). The prevalence of cases with increased CA 125 levels (>35 IU/l) in the group of stage III patients was

significantly higher than the the stage I group (p value 0.023 ; Fisher exact test).

The initial surgical approach for BOT is still under debate in contrast to invasive ovarian cancer. Laparoscopy seems to be a beneficial clinical approach for BOT as it is for benign tumors of the ovary especially for the patients who are treated conservatively (Fauvet et al., 2005; Odegaard et al., 2007). Recovery from laparoscopy is also faster along with a shorter hospital stay (Odegaard et al., 2007). In our retrospective study 45 patients out of 60 had a laparoscopy either for initial surgery or for the operative completing.

The recurrences we observed were probably unrelated to the approach itself (laparotomy or laparoscopy). The survival seems to be excellent after both types of surgical approaches. Recurrence-free survival in the group of the laparoscopy was 88.9 % and in the group of laparotomy was 88.3 % (p value, laparoscopy vs. laparotomy: 0.813). The hospital stay in the group of laparoscopy was significantly shorter (p< 0,001).

A retrospective multicenter study with 358 patients showed that the cyst rupture occurs significantly more frequently in the laparoscopy group. However, this finding had no influence on the recurrence rate (Fauvet et al., 2004). We observed tumor rupture in 11 out of total 60 patients (18.3 %). The incidence of the intraoperative rupture was not significantly higher in the group of patients treated by laparoscopy compared with laparotomy (laparoscopy: 8/45, laparotomy: 3/15; p value: 0.732) and no patient with tumor rupture had a relapse. There was also no difference in complications if the operation was performed with laparoscopy.

The strongest prognostic factor both in BOT and invasive ovarian cancer seems to be the FIGO stage at the initial diagnosis. (Lenhard et al., 2009, Tinelli et al., 2006; Ren et al., 2008). We found that the incidence of recurrence was higher among patients with advanced stage of the disease. In stage IIIc, the risk of recurrence was 10.33 times increased when compared to stage Ia. The risk of recurrence of BOT in stage Ia was significantly lower comparing to other stages (p value= 0.046). The CA- 125 level was not an independent factor for recurrence.

Borderline ovarian tumors are frequently diagnosed in women of reproductive age. Approximately one-half of such diagnoses are made in women younger than 45 years of age in our study. The treatment of this tumor, as in malignant ovarian diseases, has traditionally been radical surgery (hysterectomy with bilateral salpingo-oophorectomy) to minimize the risk of recurrence. In light of excellent prognosis of long term survival in stage I (99%)(Trimble et al., 2002), many authors have preference for conservative surgery and preserving subsequent fertility in young patiens with borderline ovarian tumors.

Recurrence is more common in patients who undergo fertility-sparing surgery than those who undergo radical surgery. However, most recurrent lesions are borderline tumors and location in the remaining ovary (Nam, 2010). In a recent review, Nam (2010) summarized studies describing outcomes of fertility sparing-surgery in patients with BOT **(Table 12).** In our study, we had 29 cases with conservative surgery (16 fertility-sparing in premenoupausal patients) and 31 cases with radical surgery. In the conservative surgery group, 5 patients (17.2 %) developed recurrence compared with 2 of 31 (6.4%) in the radical surgery group. This result shows that the risk of recurrence was increased in cases of conservative surgery but the difference was not statistically significant (p value: 0.424). This could possibly be attributed to a relatively small number of patients.

Table 12. Comparison of the outcome of fertility sparing surgery with radical surgery in patients with BOT (Nam, 2010, modified by adding results of our study)

Reference	Surgical management	Number of patients	Follow-up time (months, median)	Recurrence, *n* (%)	Location of recurrent disease at first recurrence
Ji *et al.*	Radical	70	55	3 (4)	2, abdomen; 1, omentum
	Fertility-sparing	25	88	4 (16)	3, ovary; 1, abdomen
Gotlieb *et al.*	Radical	26	57	2 (8)	2, pelvis
	Fertility-sparing	49		4 (8)	2, ipsilateral ovary; 2, contralateral ovary
Zanetta *et al*	Radical	150	70	7 (5)	NR
	Fertility-sparing	189		35 (19)	NR
Morice *et al.*	Radical	125	109	6 (5)	NR
	Fertility-sparing	49		9(18)	1, both ovary; 6, contralateral ovary; 2, NR
Romagnolo *et al.*	Radical	60	NR	4 (7)	3, pelvis; 1, NR
	Fertility-sparing	53	NR	9 (17)	2, pelvis; 3, ipsilateral ovary; 3, contralateral ovary; 1, NR
Donnez *et al.*	Radical	59	75	0 (0)	
	Fertility-sparing	16		3 (19)	3, ovary
Fauvet *et al.*	Radical	194	NR	14 (7)	NR
	Fertility-sparing	164	NR	23 (14)	NR
Park *et al.*	Radical	176	65	9 (5)	1, ovary; 1, ovary, pelvis; 1, pelvis; 2, pelvis, pelvic lymph nodes; 4, peritoneal seeding
	Fertility-sparing	184	60	9 (5)	7, ovary; 1, ovary, lung; 1, lung, pericardium
De Iaco *et al.*	Radical	83	NR	5 (6.0)	5, pelvis
	Fertility-sparing	95	NR	22 (23)	20, ovary; 1, ovary, peritoneum; 1, peritoneum
Our study 2012	***Radical***	***31***		***2***	
	Conservative	***29***		***5***	

Several authors suggest a unilateral oophorectomy instead of a cystectomy for the conservative management of BOT because the rate of recurrence after cystectomy is higher (Morice et al. 2001, Boran et al. 2005). In our study we had 5 Patients with cystectomy and 24 with salpingoophorectomy in cases which were managed conservatively. The risk of tumor rupture in cystectomy group was higher but the difference compared to the patients with oopherectomy was not significant. There was no recurrence in cases managed with cystectomy.

According to our experience the cystectomy appears to be an adequate treatment option as the oophorectomy in patients who wants to preserve their fertility.

Overall recurrence rates are often estimated to be at approximately 10 % (Lenhard at al., 2009). A German systematic review with 10971 patients showed that 37.1 % of the recurrences are diagnosed in first 2 years and 10.4 % after more than 10 years (du Bois et al., 2009). We observed a relapse rate of 11.6 % (7/60 cases). In one case a recurrence occurred in first 2 years (14 %). In 5 cases (71 %) the recurrences were between 5 and 10 years after the first diagnosis.

Investigations of the prognostic value of lymph node involvement in patients with BOT show that this is not reliable prognostic factor (Kanat et al., 2010; Lesieur et al., 2011). We had 30 cases with lymphonodectomy and only in one patient one pelvic lymphnode was positive. This patient had no recurrence since initial surgery (follow-up: 66 months).

7. Conclusion

The retrospective analysis of all cases with BOT (01/1996-03/2011) at our hospital provides additional evidence that laparoscopic management of BOT is a feasible and safe method for fertility preserving surgery as well as for radical surgery including a complete staging. The surgical access of the operation in our cohort of this rare disease with a relatively long follow up had no influence on the recurrence so far. Laparoscopy resulted in a statistically significant shorter hospital stay in comparison to patient population managed by laparotomy. Fertility sparing surgery of women in reproductive age could be appropriate treatment option in the management of BOT. However, patients should be informed about the increased recurrence risk due to the residual ovarian tissue. These patients could be enrolled in an automatic recall programm for completion surgery after family planning is completed.

The removal of ovarian and omental tissue may lead to a longer disease free survival in the female population who have fulfilled their family planning and live beyond reporoductive age. Hence a second look surgery with completion of staging to resect the tissue with increased risk for recurrent BOT may prove to be beneficial.

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9. Supplement

Abreviations

AE	Adnexectomy
App	Appendectomy
HE	Hysterectomy
LSK	Laparoscopy
LAP	Laparotomy
LNE	Lymphonodectomy
uni	unilateral
bil	bilateral
pel	pelvic
pa	paraortic
Li	left
re	right
BOT	Borderline ovarian tumor

Presented Abstracts

- Dogan, A. Winzer, O. Camara, I. B. Runnebaum „Laparoskopische Operationen von borderline Ovarialtumoren über 10 Jahre“
  AGE Congress, Münster 2010.
- Dogan A., Camara O., Runnebaum I. B**.** „Fertility sparing surgery of borderline ovarian tumors: Laparoscopy vs. laparotomy”
  DGGG Congress, München 2010
- Dogan A., Camara O., Runnebaum I. B. „ Over ten years follow up of laparoscopic treatment of borderline ovarian tumors”
  ESGE Congress, Barcelona 2010

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Acknowledgments

Above and beyond the words and the extent of any event in my life, I am eternally blessed with the love and care my parents have bestowed upon me with so much dedication. I am deeply grateful for their love and support thoughout my life. Also I am indebted to Professor Dr. med. Ingo Runnebaum for his contious help, mentorship and expert opion to bring this doctorate thesis in fruition. Dr. Michels of the statistic's division at the University Jena has contributed to the analysis of data and I am extremely grateful for his expert support. This work would have not been completed without the love and constant motivation of my wife Dr. Agnieszka Paradowska-Dogan.